Physiology of blood Erythrocytes- 2

Dr. Nasser Rizk MD, PhD

2006

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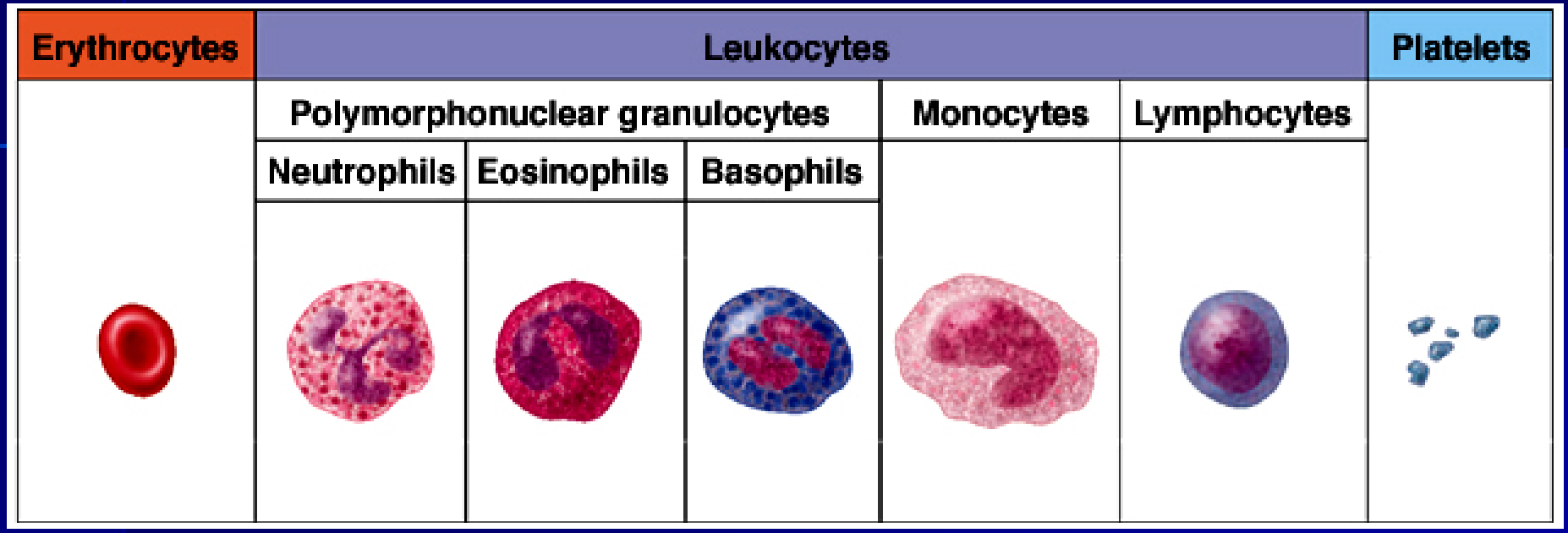
Figure 12-70



The major forms of "cells" in the blood. Among these, only the leukocytes are true cells with nuclei.

Blood Cells and Platelets

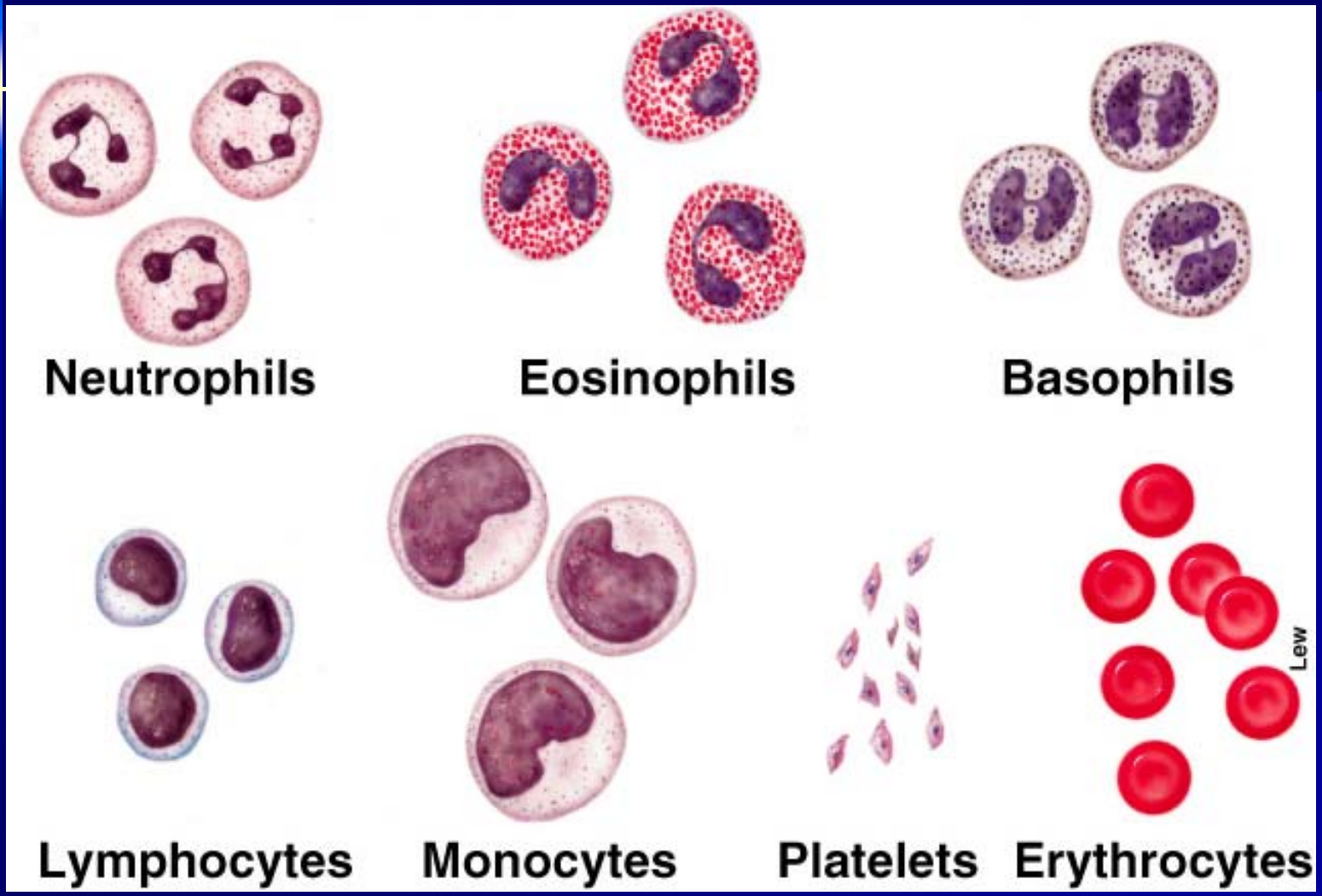


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TABLE 12–12 Numbers and Distributions of Erythrocytes, Leukocytes, and Platelets in Normal Human Blood

Total erythrocytes = 5,000,000 per mm^3 of blood
Total leukocytes = 7000 per mm^3 of blood
- Percent of total leukocytes:
  - Polymorphonuclear granulocytes
    - Neutrophils 50–70%
    - Eosinophils 1–4%
    - Basophils 0.1%
  - Monocytes 2–8%
  - Lymphocytes 20–40%

Total platelets = 250,000 per mm^3 of blood

Erythrocytes

- Flattened biconcave discs.
- Provide increased surface area through which gas can diffuse.
- Lack nuclei and mitochondria.
  - Half-life ~ 120 days.
- Each RBC contains 280 million hemoglobin with 4 heme chains (contain iron).
- Removed from circulation by phagocytic cells in liver, spleen, and bone marrow.

Red blood cells "Erythrocytes"

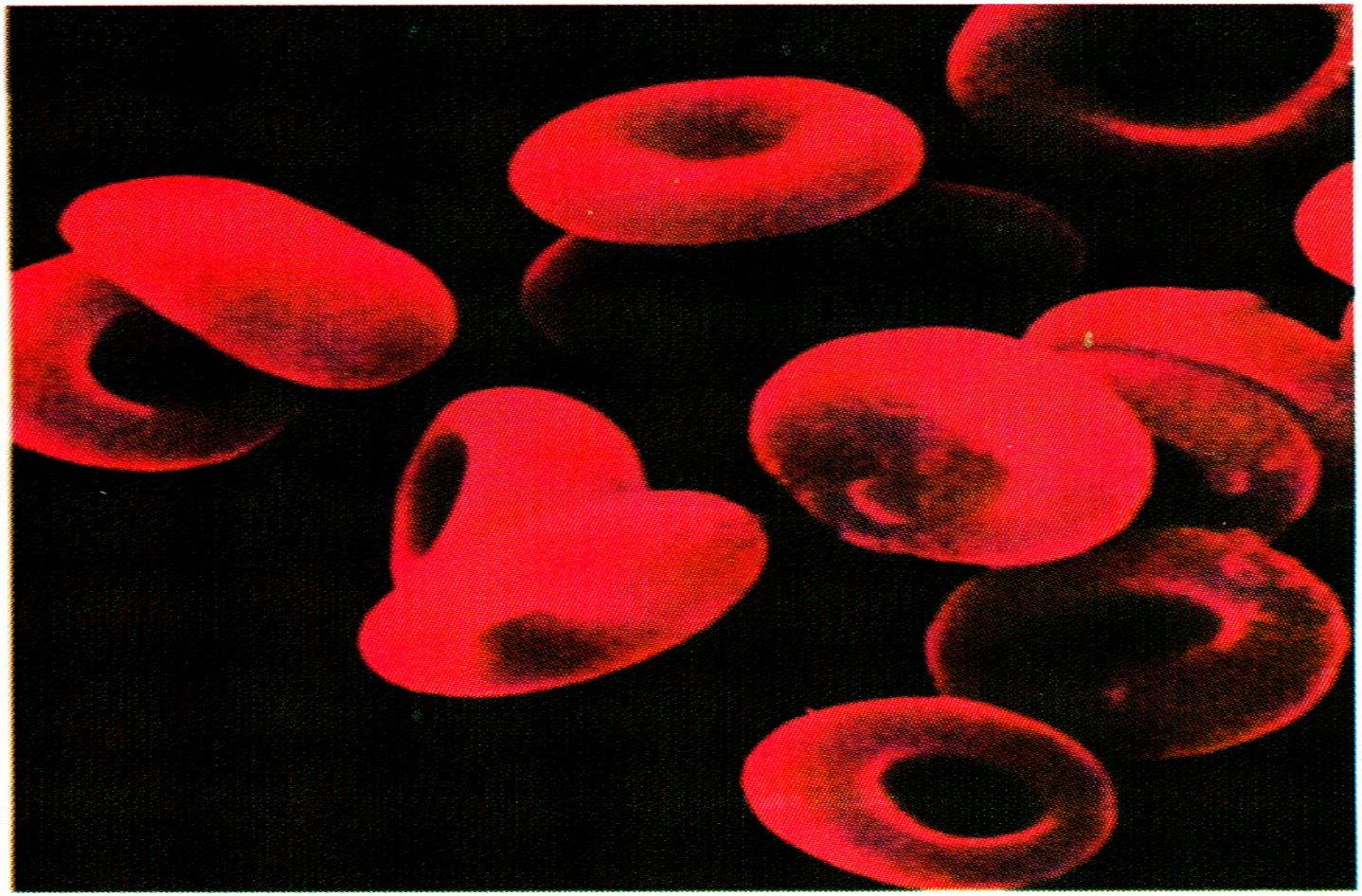
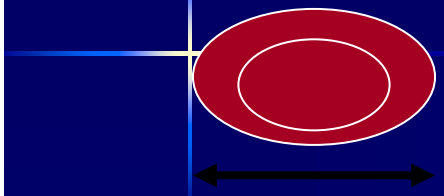


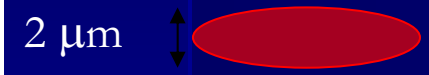
Figure 17-4 Erythrocytes. Color-enhanced scanning electron micrograph shows normal erythrocytes. (From Ishihara: *Tests for color blindness.*)

Anatomy of RBC

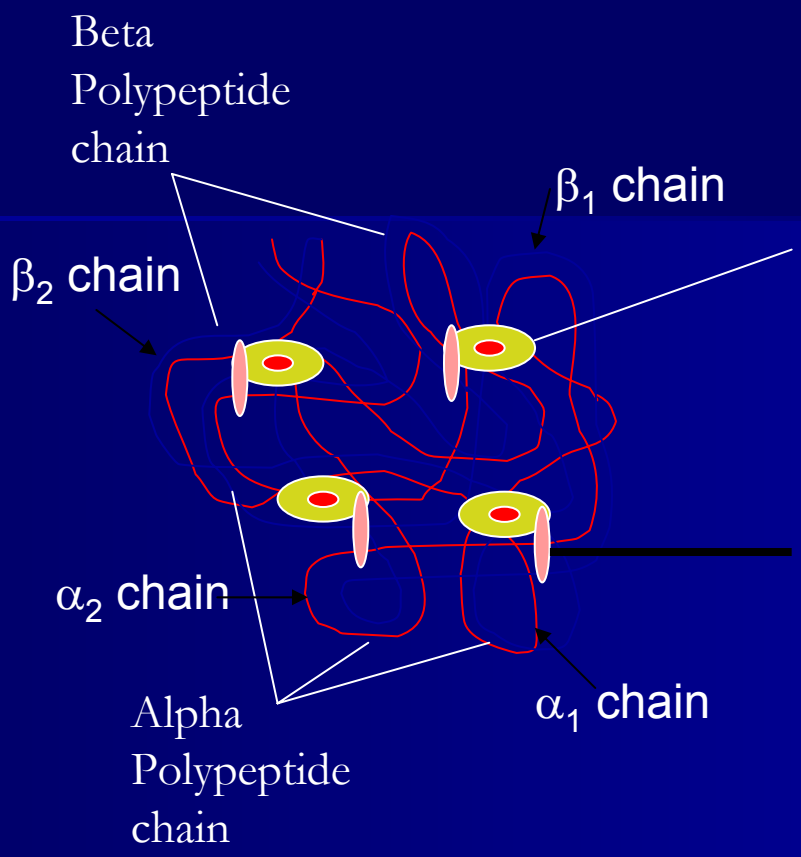


Diameter = 7.5-8μm

Surface view



Sectioned view



RBC shape

Hemoglobin molecule

Anatomy of RBCs

1. **Biconcave discs**
2. **Non-nucleated**
3. **Diameter: 8μm Thickness: 2.0 μm**
4. **Contain: Hemoglobin (33%) of cell weight = 29 Pg**
5. **Number: average in**

♂: 5.4 million/μl ♀: 4.8 million/μl

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1. Synthesis: Bone marrow (adults)
2. Life span: 120 days

Physiology of RBC

- Main function of RBC: carriage of blood gases **mainly** **O2** (99%) and to less extent CO2 (30%)

  by the hemoglobin carrier.

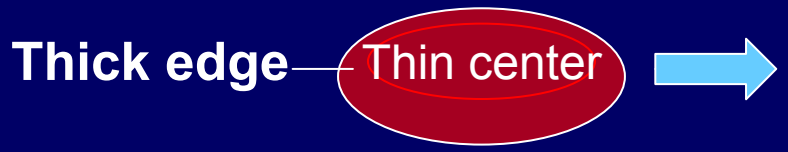
- Adaptation of RBC to transport O2:

1- No nucleus

2-Lack of mitochondria (RBC not utilize O2 for energy production)

3- Greater surface area for its volume

Unique shape of RBC:



4- Shape of RBC:

Change passively through blood capillaries $< 7.5\ \mu m$

It is inherent flexibility due to **Spectrin protein** in its Plasma Membrane

It allows the RBC to accommodate change from biconcave shape to small cup-shape under : Shearing stress, high blood pressure, passage through microcirculation.

Hemoglobin molecule

- Consists of : 1- protein called globin

2- Non-protein pigment [heme]:

Each heme is present in one peptide chain and

contains an iron {Fe++} that combines reversibly

with one molecule of O2

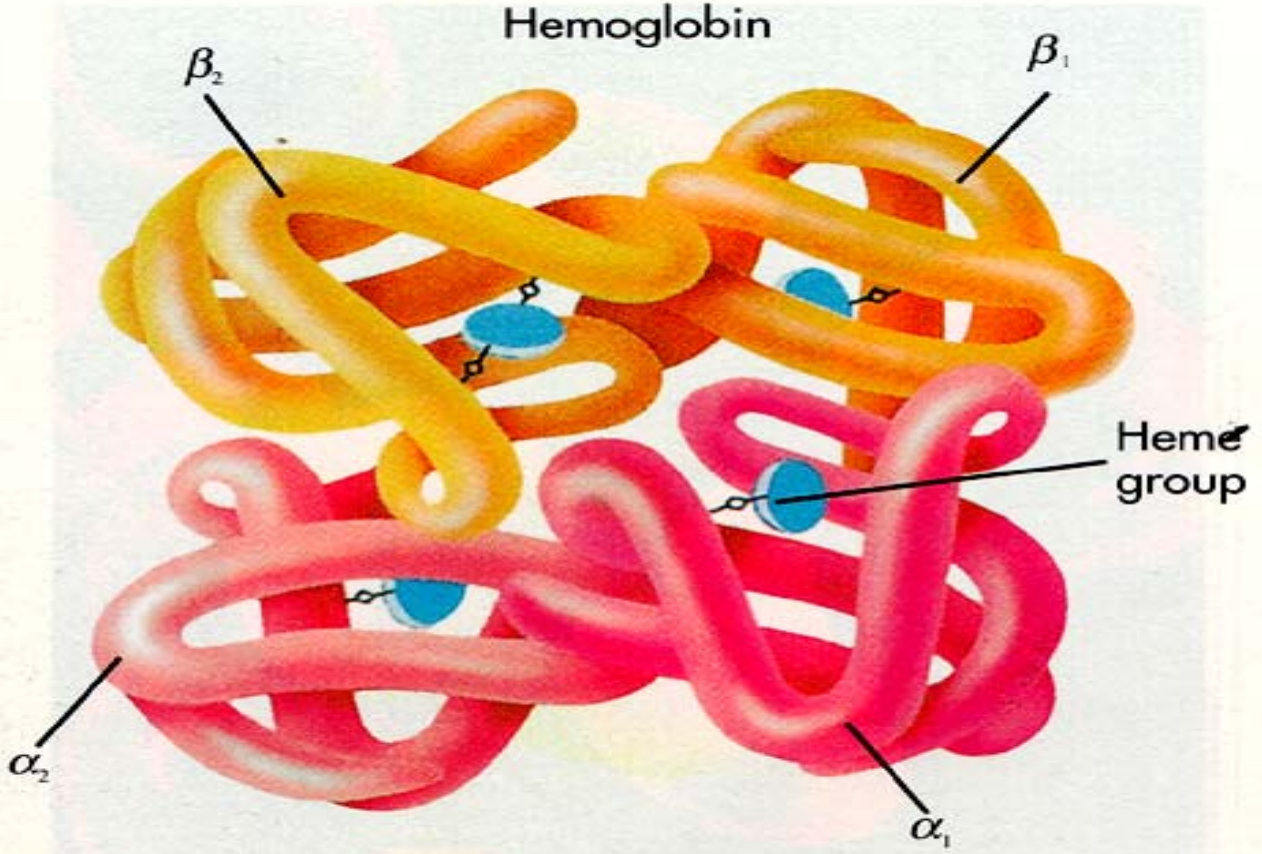


Figure 17-5 **Hemoglobin.** Four protein chains (globins), each with a heme group, form a hemoglobin molecule. Each heme contains one iron atom.

- The Hb molecule combine maximally with 4 molecules of O_2 in a cascade manner (100% saturated), by

- **Oxygenation** reaction, each binding facilitates further binding of O_2,
- **not oxidation** reaction.

- **Saturation of Hb**: refers to the number of O_2 molecules combined with Hb.

- 50 % saturation: means that Hb binds with 2 molecules of O_2.

Functions of Red Blood Cells

- **1-Transport of O_2** (99%) inside RBC, 1% in plasma. **(Main function)**

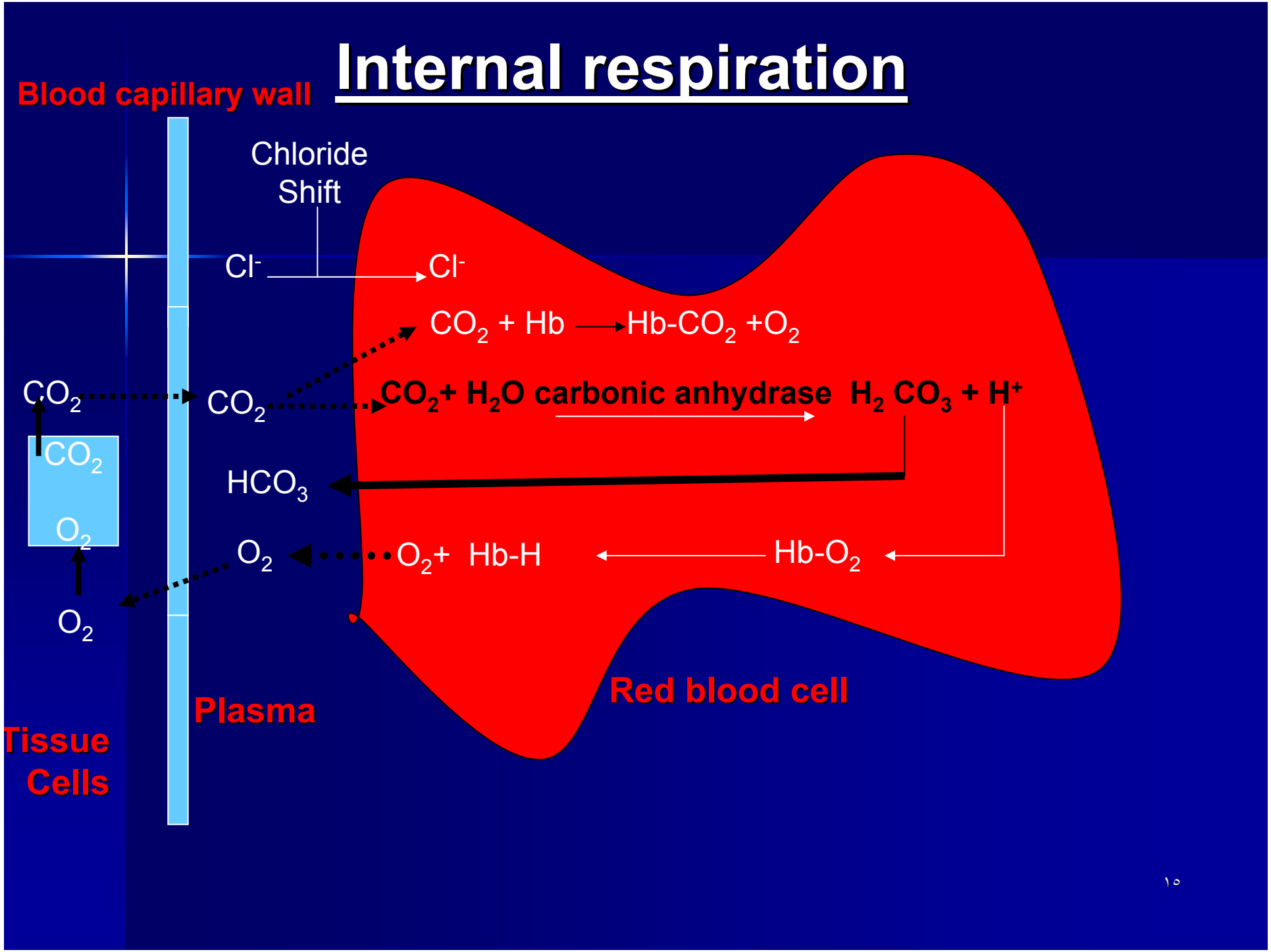
From lung to tissues (Hb dependent)

- 2- **Transport of CO_2** (13% with Hb)

From tissues to lung to atmosphere, it depends on Hb and Carbonic anhydrase enzyme.

- 3- It has a role in **acid-base balance** through formation of bicarbonate HCO_3^-

Internal respiration



- 4- **Regulate blood flow**

- 5- **Regulation of blood pressure**. How?
- **Answer:**

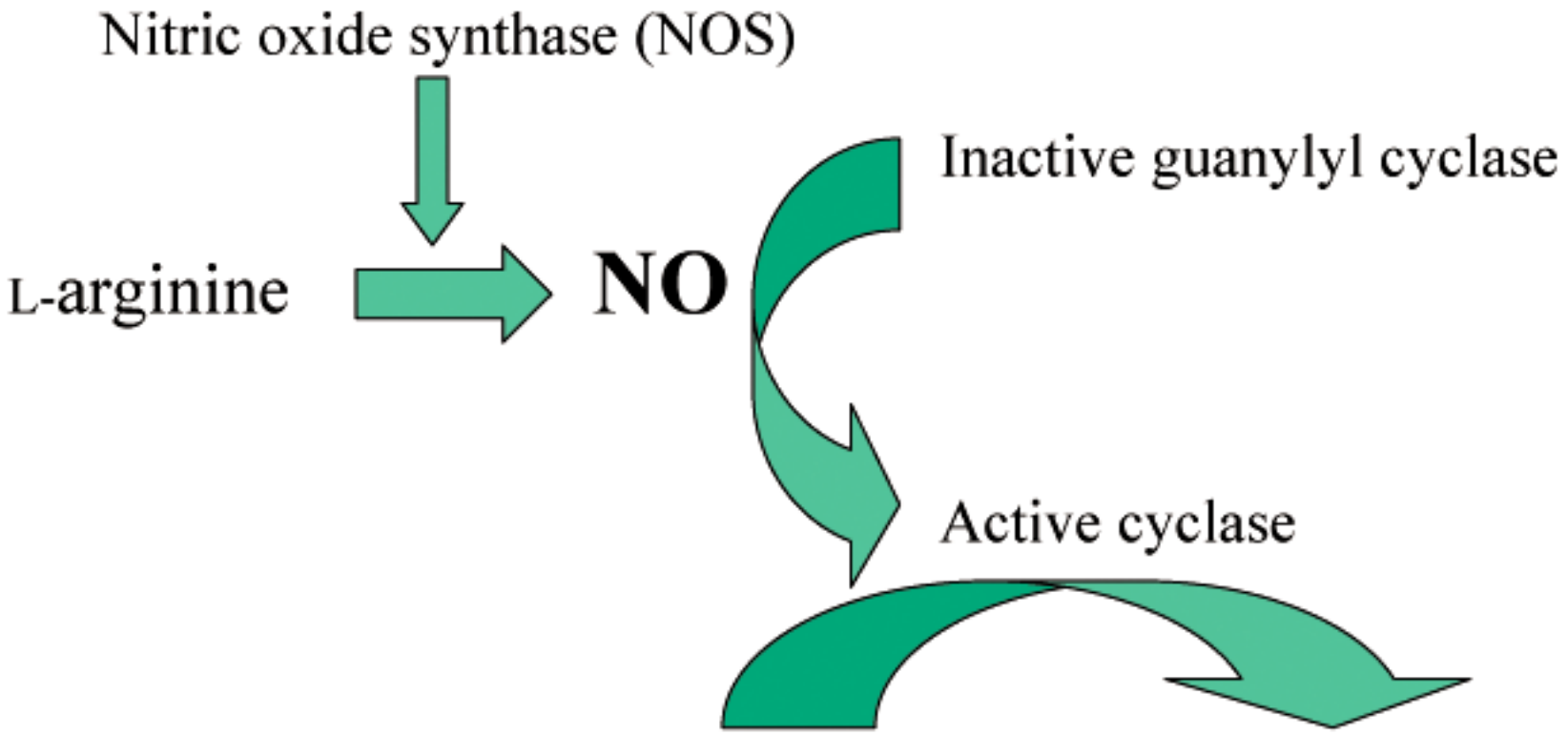
NO (nitric oxide) released by endothelial cells

Binds Hb. Then Hb under conditions releases

NO causes vasodilatation and increase blood

flow and decrease blood pressure

Nitric oxide production in vascular endothelial cells



Nobel Prize 1998
R. Furchgott
F. Murad
L. Ignarro

Hematopoiesis

- Undifferentiated cells gradually differentiate to become stem cells, that form blood cells.
- Occurs in myeloid tissue (bone marrow of long bones) and lymphoid tissue.
- 2 types of Hematopoiesis:
  - Erythropoiesis:
    - Formation of RBCs.
  - Leukopoiesis:
    - Formation of WBCs.

Erythropoisesis

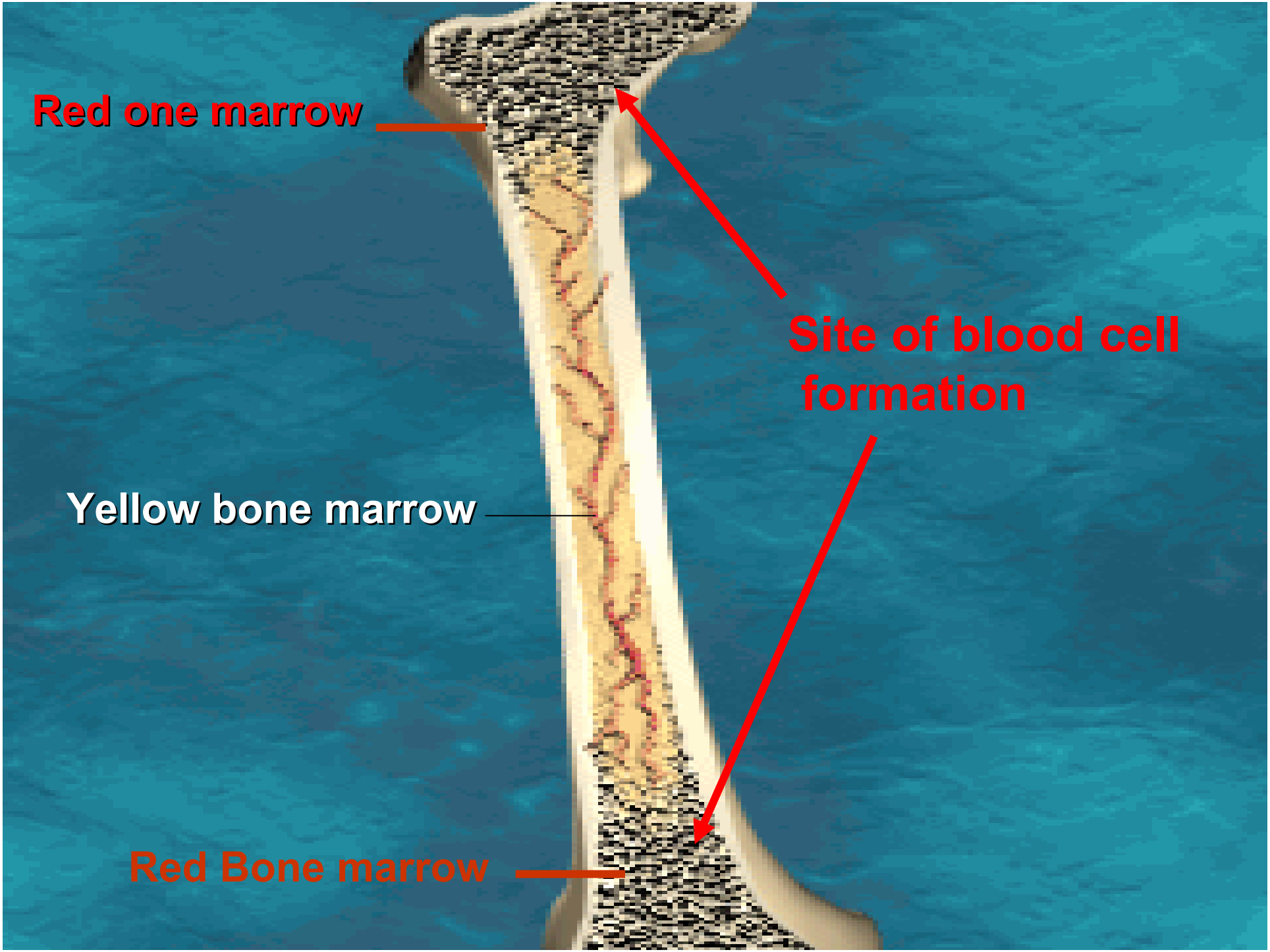
The process of

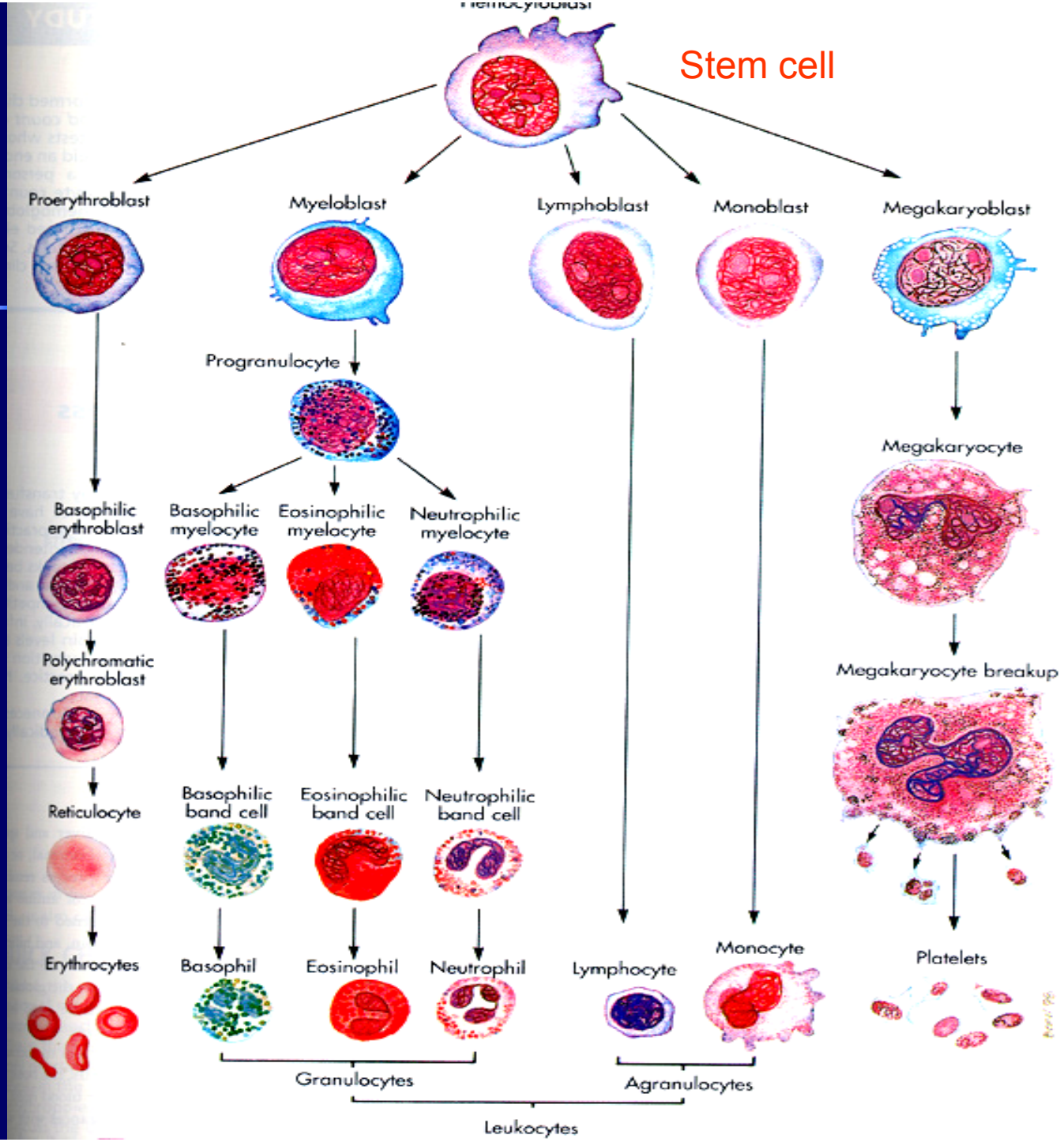
Red blood cell Formation

Rate of:

RBC synthesis = RBC destruction

Relatively constant number of RBC


Red one marrow
Site of blood cell formation
Yellow bone marrow
Red Bone marrow


Stem cell
Proerythroblast
Myeloblast
Lymphoblast
Monoblast
Megakaryoblast
Progranulocyte
Megakaryocyte
Basophilic erythroblast
Basophilic myelocyte
Eosinophilic myelocyte
Neutrophilic myelocyte
Megakaryocyte breakup
Polychromatic erythroblast
Reticulocyte
Basophilic band cell
Eosinophilic band cell
Neutrophilic band cell
Erythrocytes
Basophil
Eosinophil
Neutrophil
Lymphocyte
Monocyte
Platelets
Granulocytes
Agranulocytes
Leukocytes

Mechanism of Erythropoisesis

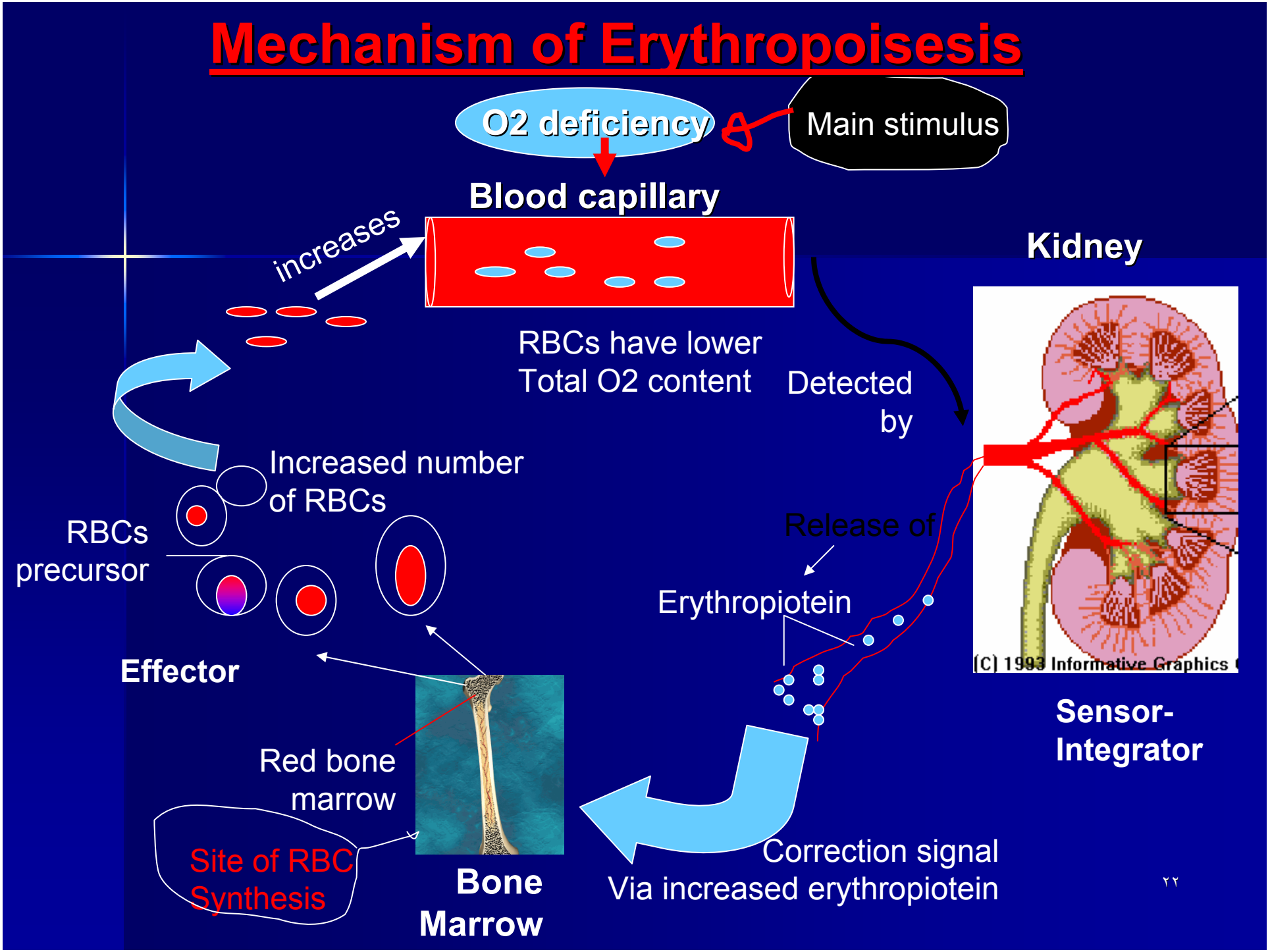


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Figure 12-68

The availability of dietary iron can be a limiting factor in erythropoiesis, so storage and recycling mechanisms are highly developed in humans, as protection from anemia.

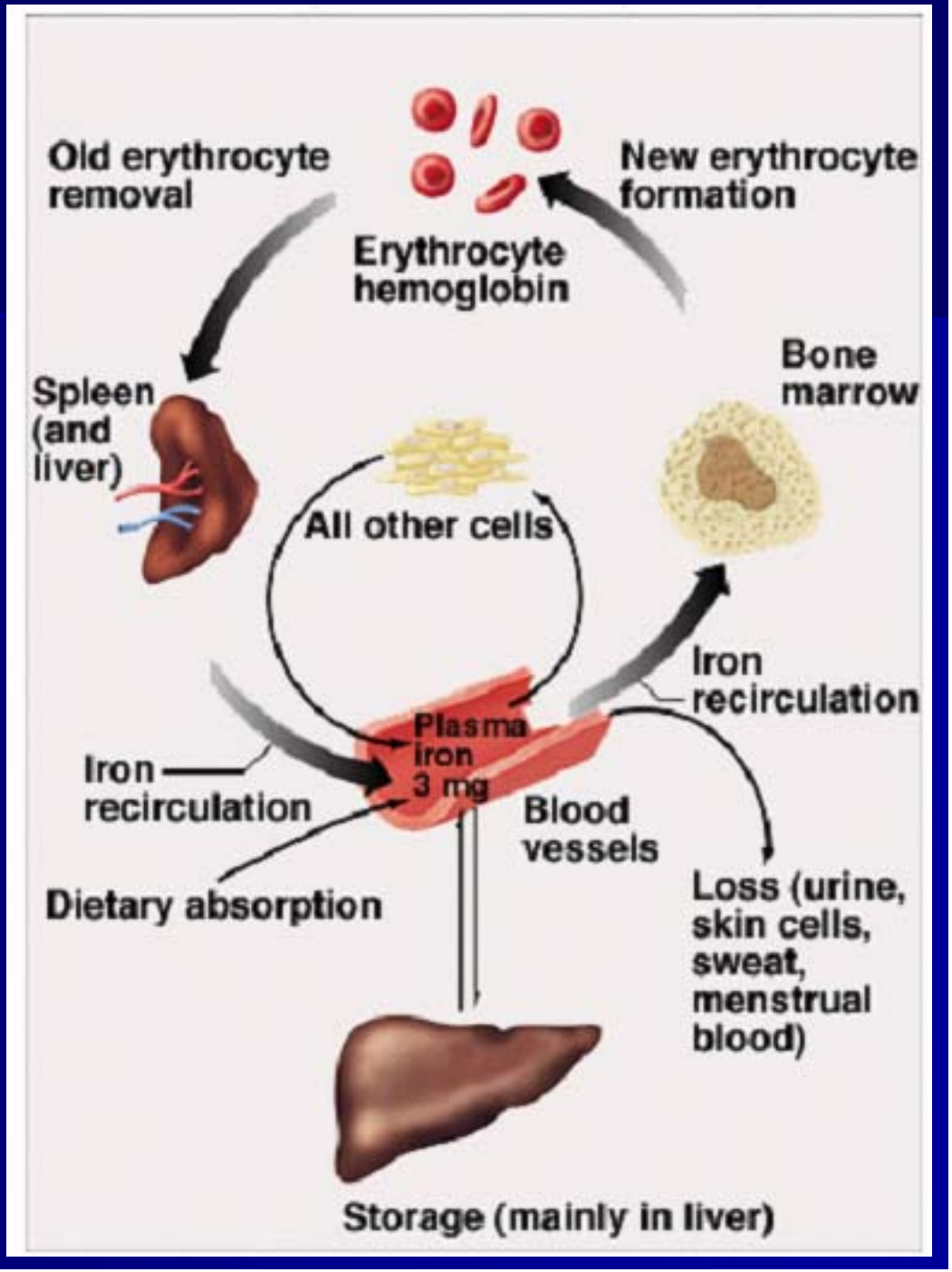

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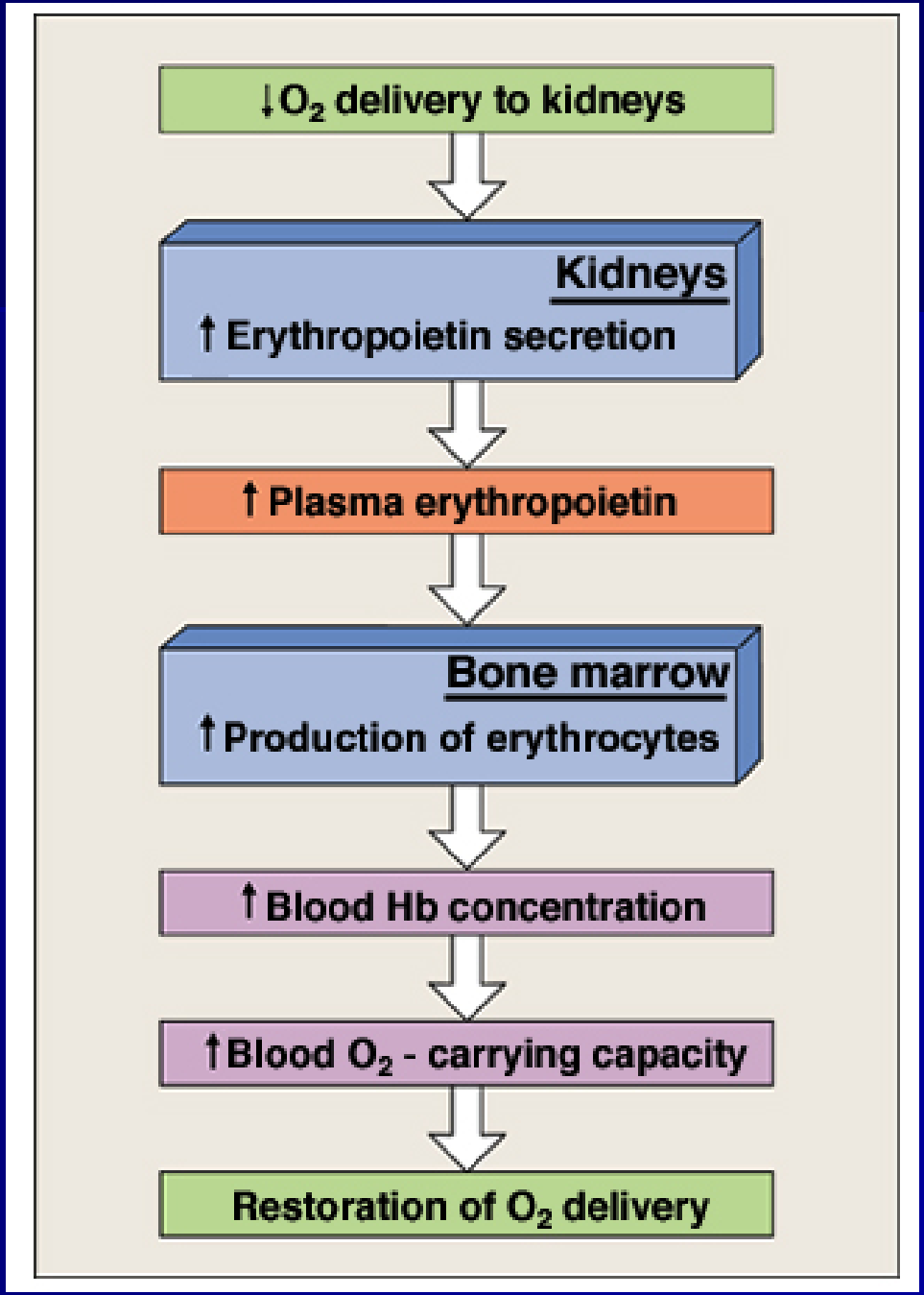
Figure 12-69

Erythropoiesis is hormonally regulated:

decreased oxygen delivery to the kidney causes the secretion of erythropoietin, which activates receptors in bone marrow, leading to an increase in the rate of erythropoiesis.



Erythropoiesis (continued)

- Erythropoisesis: formation of new RBCs

- **1-Nutriotional requirements:**

Iron (iron-deficiency anemia)

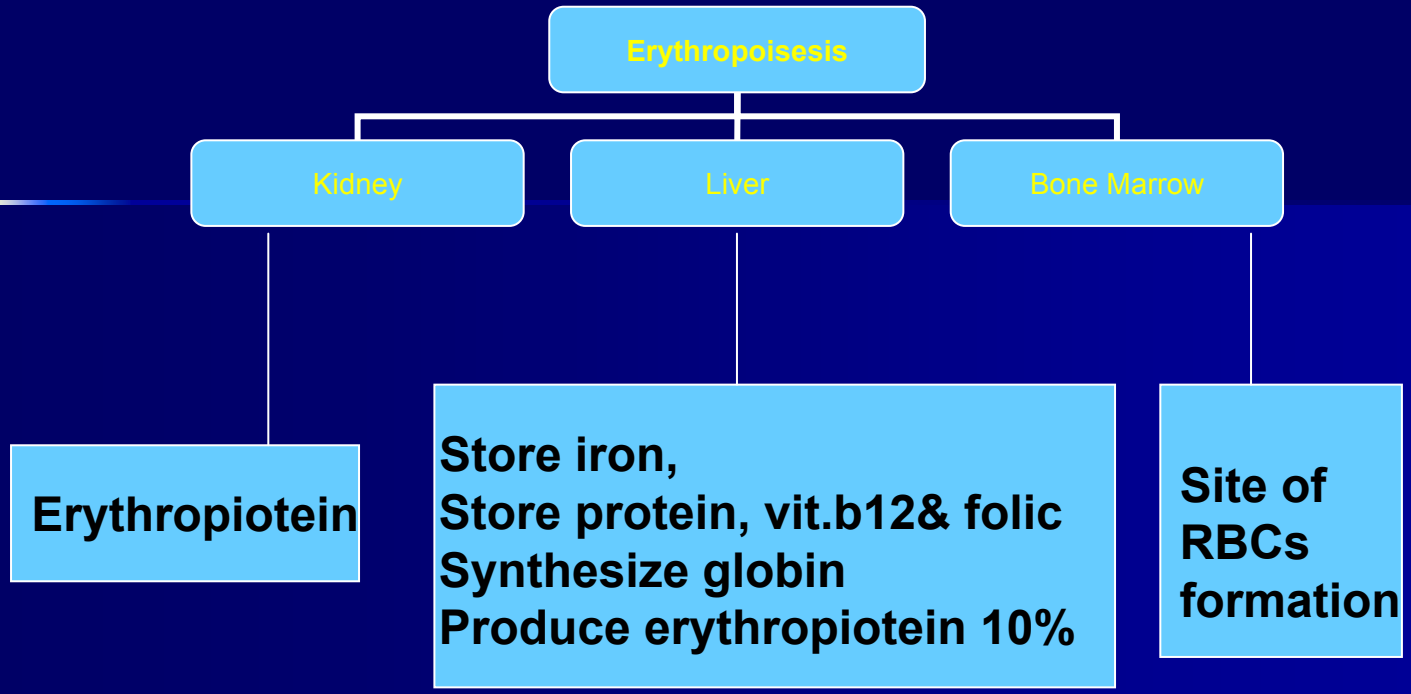
Vitamins (B12 and folic acid)------Maturation failure anemia

Protein meal rich in high biological value of A.A.

Other factors: Cu, Iodine, trace elements

Vitamin B complex and Vitamin C

- 2-organs involved in erythropoisesis:



- **3- Other organs involved:**

Stomach: B12 absorption

Small Intestine: absorption of Iron, vitamins, and A.A

Lung, heart, macrophage cells in other organs and lymph nodes

- **Endocring glands involved in erythropoisesis**
- **1- Thyroid gland: ++ Metabolic rate**

- **2- Adrenal glands:**

Androgen hormones stimulate RBC formation (♂ RBC >♀ RBC). Glucocorticoids :++

Summary: RBC formation is a vital process involves interactions of different organs and systems to produce adequate number with sufficient Hb.

RBC number and Hb estimation: indicates activity of different body systems.

Erythropoiesis (summary)

- Active process.
  - 2.5 million RBCs are produced every second.
- Primary regulator is erythropoietin.
  - Binds to membrane receptors of cells that will become erythroblasts.
  - Erythroblasts transform into normoblasts.
  - Normoblasts lose their nuclei to become reticulocytes.
  - Reticulocytes change into mature RBCs.
    - Stimulates cell division.
- Old RBCs are destroyed in spleen and liver.
  - Iron recycled back to myeloid tissue to be reused in hemoglobin production.
- Need iron, vitamin B_{12} and folic acid for synthesis.

Destruction of RBCs

- 1- Old RBCs without nucleus can't synthesize new components
- 2- With aging, its plasma membrane more fragile- burst, → rupture esp. in sinuses of spleen, L.N, liver, and bone marrow.
- 3- The Macrophage cells inside these structures break hemoglobin into

Heme part | **Globin part**

Life cycle of red blood cells

Aged RBC 120 days

Site of destruction

Stercobilin

blood

kidney

Bilirubin excreted Into intestine as a part of bile

liver

Biliverdin

Bilirubin

Macrophage

Hemoglobin

Heme

Globin

iron

stored

synthesis

Amino acids

Liver

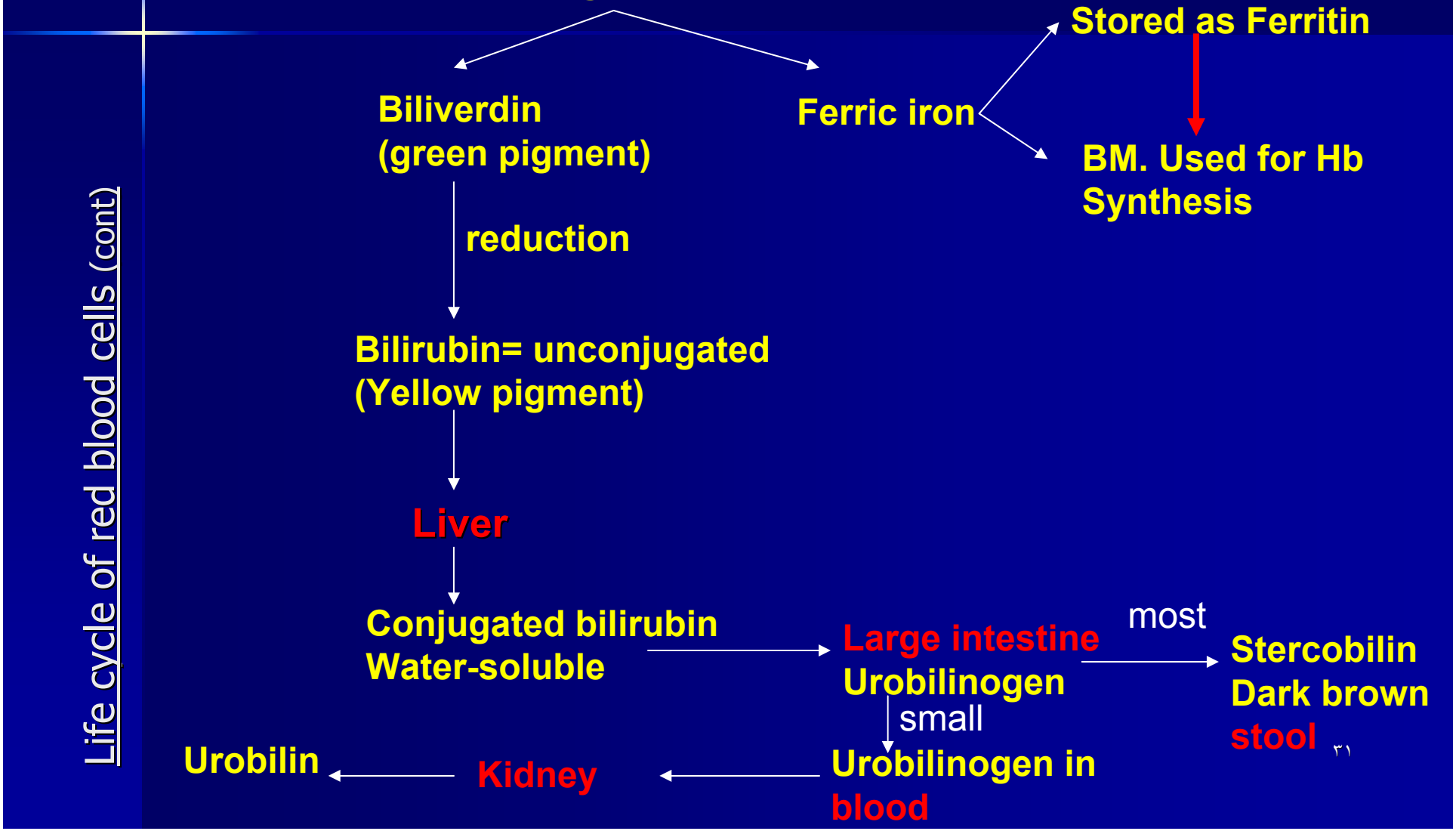
Red Bone marrow

Spleen

Macrophage in
Spleen
Liver
Lymph nodes
Bone marrow
etc

•4- Globin → amino acids (stored or used for new protein synthesis.

•5- Heme part splits to give:



Clinical application

- **Anemia**: a decrease in;

1- RBC number or/and

2- Hb content

Below the normal for that sex and age.

Effects of anemia: due to decrease O2 supply to tissues

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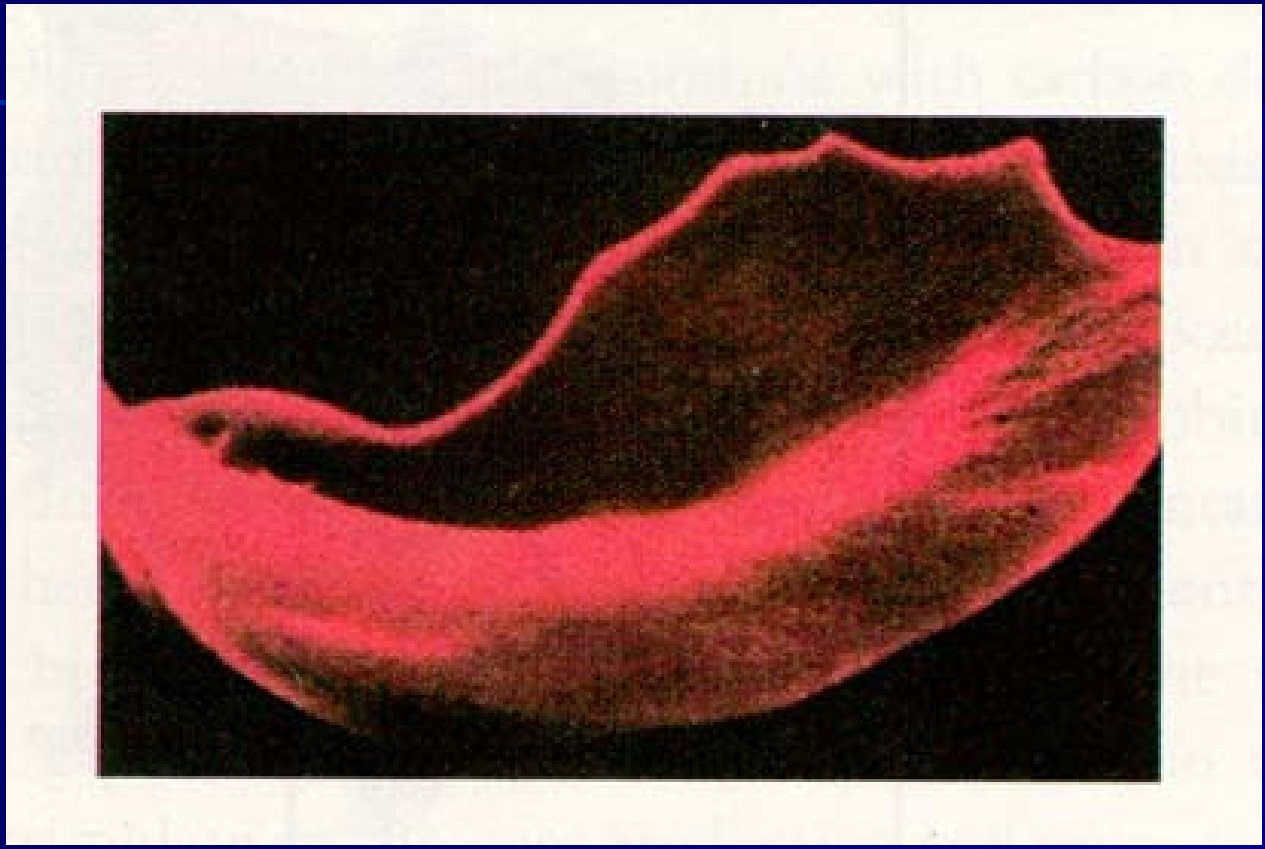
TABLE 12–11 Major Causes of Anemia

1. Dietary deficiencies of iron (***iron-deficiency anemia***), vitamin B_{12}, or folic acid
2. Bone marrow failure due to toxic drugs or cancer
3. Blood loss from the body (***hemorrhage***) leading to iron deficiency
4. Inadequate secretion of erythropoietin in kidney disease
5. Excessive destruction of erythrocytes (for example, sickle-cell anemia)

Effects of anemia

- 1- Fatigue, muscle weakness
- 2- Mental effects: lack of concentration and dizziness , even faintining
- 3- CVS effects: tachycardia, palpitation, heart failure if not treated
- 4 nausea & anorexia
- 5- Retarded growth in children



Sickle cell shape RBC

Polycythemia

- Increase Red blood cell count above normal
- Types:
- 1-Relative: fluid loss ad plasma loss in burns, dehydration
- 2- Absolute: Actual increase in RBC/Hb
- **Effects:**
- 1- Increased Blood viscosity…….load on heart…..++cardiac work……..heart failure

- **2- increase incidence of hyperviscosity…..thrombosis and obstruction of different blood vessels**

- 3- **decreased blood flow to tissues and Decreased delivery of O2 to tissues**

- 4- ++ **PCV**

Treatment: aim to remove RBC by;
phlebotomy, blood donation

Questions

- Summarize the production, life span, and destruction of RBCs?
- What are the routes of iron gain, loss and distribution?
- Describe Control of erythropoietin secretion and effect?
- Differentiate between biliverdin and bilirubin?